

Correspondence

Improved survival with amiodarone in patients with hypertrophic cardiomyopathy and ventricular tachycardia

Sir,

In their recent paper (1985; 53: 412-6) McKenna *et al* conclude that amiodarone may prevent sudden death in patients with hypertrophic cardiomyopathy. They studied patients with ventricular tachycardia recorded on Holter monitoring. Of 24 patients not treated with amiodarone (historical controls) five died suddenly during a three year follow up while all 21 patients on amiodarone survived for at least three years. The implications of this observation make careful examination of potential confounding factors essential. Information is required about the control group that is not explicit in the paper nor in a previous report about these patients.¹

The crucial issue is the drug treatment with "conventional antiarrhythmic agent" and the relation between the use of individual drugs and sudden death. McKenna *et al* state that "we entered seven of the patients with ventricular tachycardia (included in the conventional treatment groups) into a comparative study of the antiarrhythmic effect of disopyramide and mexiletine" ... "four of the seven died suddenly during treatment". Apart from this group there was therefore only one sudden death in the other 17 patients with ventricular tachycardia. Were these 17 also treated with mexiletine or disopyramide or just with quinidine, and how were the seven selected for the antiarrhythmic study? That these deaths were not typical of the natural history of hypertrophic cardiomyopathy is suggested in the earlier paper by the greater ages of these patients and they imply a more severe functional limitation than was found in 32 patients who died in the total series. Could it be that these older, more severely affected patients are particularly at risk from electrophysiological or mechanical instability when a particular antiarrhythmic agent is added to high dose beta blockade? This risk would not necessarily be marked by observable QT prolongation or premonitory arrhythmia.

On the data given by McKenna *et al* it could be concluded that mexiletine or disopyramide was responsible for most of the observed mortality and that the main benefit of amiodarone was in saving patients from being subjected to the toxic effects of these agents.

To clarify the situation it would be helpful to know what drugs each patient who died was taking (and for how long), the numbers of the survivors treated with similar drugs or combinations, and in which patients treatment was apparently successful (that is, did any of these patients die?). McKenna *et al* may also be able to supply from their own extensive experience or from elsewhere a more valid group for comparison with the amiodarone group—namely patients with hypertrophic cardiomyopathy and ventricular tachycardia who were not treated with antiarrhythmic agents but were treated with adequate beta blockade. Alternatively they could attempt to show that the overall three year mortality associated with the policy of amiodarone treatment of ventricular tachycardia is significantly different from that associated with treatment only by beta blocking or calcium antagonists drugs. Until this can be done their assertion that "a randomised prospective study" ... "was never feasible" is only justified in relation to comparison with the other antiarrhythmic agents. Long term treatment with amiodarone is not a trivial intervention and before it is applied to all patients with hypertrophic cardiomyopathy and ventricular tachycardias (except for relief of severe symptoms) a properly designed placebo controlled trial must be undertaken.

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Reference

- 1 McKenna WJ, England D, Doi YL, Deanfield JE, Oakley C, Goodwin JF. Arrhythmia in hypertrophic cardiomyopathy. I: Influence on prognosis. *Br Heart J* 1981; 46: 168-72.

This letter was shown to Dr McKenna, who replies as follows:

Sir,

In his letter Dr Crick raises the possibility that the class I antiarrhythmic agents used in the treatment of 24 consecutive patients with hypertrophic cardio-

myopathy and ventricular tachycardia may have adversely affected prognosis.¹ The available evidence does not suggest this, but the possibility cannot be excluded. The arrhythmogenic effects of disopyramide, mexiletine, and quinidine are well known; 22 of the 24 patients had 12 lead electrocardiograms and 48 hour ambulatory electrocardiographic monitoring performed during treatment and we did not see changes that suggested an arrhythmogenic effect such as elongation of the QT interval or multiform ventricular tachycardia. In this regard our data are similar to those reported by Maron *et al* for a study in which four of 19 patients who were receiving class I antiarrhythmic agents for the treatment of asymptomatic paroxysmal ventricular tachycardia died suddenly² without evidence of an arrhythmogenic effect of treatment (B J Maron, personal communication). Of the five patients with ventricular tachycardia who died suddenly in our study, three were on disopyramide (400 or 600 mg daily), one was on quinidine (500 mg daily), and the other had been treated with disopyramide and mexiletine (both were poorly tolerated) but was not on antiarrhythmic agents when death occurred. All of the survivors who had ventricular tachycardia received at least one class I antiarrhythmic agent. (These agents were never used in combination.) The drugs were changed according to their efficacy and side effects. The drug which was used for the longest period was disopyramide in 10, quinidine in eight, and mexiletine in four.

Before the recognition of asymptomatic ventricular arrhythmia and the use of class I antiarrhythmic agents, the annual mortality from sudden death in adults with hypertrophic cardiomyopathy was 2.6% (254 patients).³ Details of these patients have been published; in brief, the majority received propranolol (mean 220 mg daily) and few were on specifically antiarrhythmic drugs, usually for control of symptomatic supraventricular arrhythmia.³ With the widespread use of ambulatory electrocardiographic monitoring the high frequency of asymptomatic ventricular arrhythmia was recognised.^{4,5} During the period (1977 to 1980) when class I antiarrhythmic agents were used to treat paroxysmal ventricular tachycardia the overall annual mortality from sudden death was reported to be 2.7% (86 patients)⁵ and 2.4% (83 patients).² In these two predominantly adult populations the finding of ventricular tachycardia during electrocardiographic monitoring was associated with sudden death. The similar annual mortality before and after the treatment of ventricular tachycardia with class I antiarrhythmic agents does not support the suggestion of an occult arrhythmogenic effect.

Since 1980 we have routinely used amiodarone to

treat refractory supraventricular arrhythmia and paroxysmal non-sustained ventricular tachycardia. Our experience in the first 82 patients is outlined in our paper; the annual mortality from sudden death was 0.8%.¹ During the entire period under examination we used the same approach to treat symptoms, and the clinical, echocardiographic, and haemodynamic characteristics of the two consecutive patient populations were similar. These data on annual mortality do not suggest an adverse effect on prognosis by class I antiarrhythmic agents and they support the finding of improved survival during amiodarone treatment of patients with hypertrophic cardiomyopathy and ventricular tachycardia. We are well aware that long term treatment with amiodarone is associated with side effects, some of which are serious.⁶ For this reason we have been hesitant to assess the effect of amiodarone on sudden death in children with hypertrophic cardiomyopathy. This age group is at greatest risk of sudden death.⁷

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References

- 1 McKenna WJ, Oakley CM, Krikler DM, Goodwin JF. Improved survival with amiodarone in patients with hypertrophic cardiomyopathy and ventricular tachycardia. *Br Heart J* 1985; 53: 412-6.
- 2 Maron BJ, Savage DD, Wolfson JK *et al*. Prognostic significance of 24h ambulatory electrocardiographic monitoring in patients with hypertrophic cardiomyopathy: a prospective study. *Am J Cardiol* 1981; 48: 252-7.
- 3 McKenna WJ, Deanfield J, Faruqi A, England D, Oakley CM, Goodwin JF. Prognosis in hypertrophic cardiomyopathy: role of age and clinical, electrocardiographic and hemodynamic features. *Am J Cardiol* 1981; 47: 532-8.
- 4 Savage DD, Seides SF, Maron BJ, Myers DJ, Epstein SE. Prevalence of arrhythmias during 24 hour electrocardiographic monitoring and exercise testing in patients with obstructive and nonobstructive hypertrophic cardiomyopathy. *Circulation* 1979; 59: 866-75.
- 5 McKenna WJ, England D, Doi YL, Deanfield JE, Oakley CM, Goodwin JF. Arrhythmia in hypertrophic cardiomyopathy: I. Influence on prognosis. *Br Heart J* 1981; 46: 168-72.
- 6 Harris L, McKenna WJ, Rowland E, Holt DW, Storey GCA, Krikler DM. Side effects of long-term amiodarone therapy. *Circulation* 1983; 67: 45-51.
- 7 McKenna WJ, Deanfield JE. Hypertrophic cardiomyopathy: an important cause of sudden death. *Arch Dis Child* 1984; 59: 971-5.